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POSTER PRESENTATION

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# Corticosterone enhances CSD susceptibility via glucocorticoid receptor activation in familial hemiplegic migraine 1 *Cacna1a* knock-in mice

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## Introduction

FHM1 mutant mice carrying the R192Q gain-of-function mutation in *CaV2.1* (P/Q-type) calcium channels display enhanced glutamatergic transmission and increased propensity for cortical spreading depression (CSD;1,2). Corticosteroids released after stress also enhance glutamatergic transmission but the relationship between stress and migraine is not well understood.

## Objectives

We aimed to investigate the acute effects of corticosterone and the role of GR activation on CSD susceptibility in FHM1 R192Q knock-in mice.

## Methods

Corticosterone (20 mg/kg) or vehicle was injected subcutaneously 4 hours before CSD frequency recordings were carried out in FHM1 R192Q mice. A subgroup of mice was injected with the glucocorticoid receptor antagonist mifepristone 50 minutes before corticosterone/vehicle injection.

## Results

Corticosterone injection increased CSD frequency in FHM1 mice compared to vehicle-injected controls but not in wild-types. Pretreatment with mifepristone reduced CSD frequency to the level of vehicle-injected controls. Baseline corticosterone plasma levels were similar in WT and FHM1 mice, while 3 hours after corticosterone administration corticosterone plasma levels were strongly

elevated to comparable levels in both WT and FHM1 mice.

## Conclusion

These data suggest that combined effects of glucocorticoid receptor activation and the FHM1 R192Q *CaV2.1* gain-of-function mutation on excitatory neurotransmission may play a role in proposed effects of stress on migraine attacks.

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